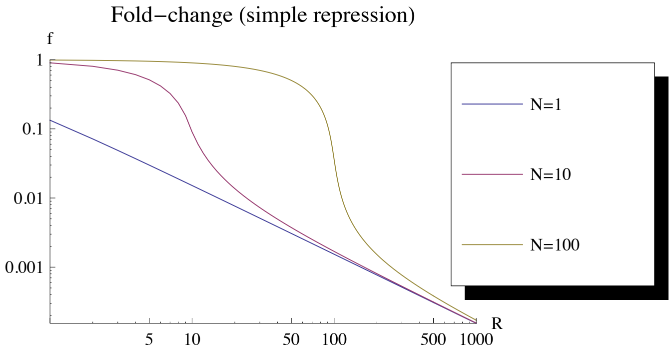
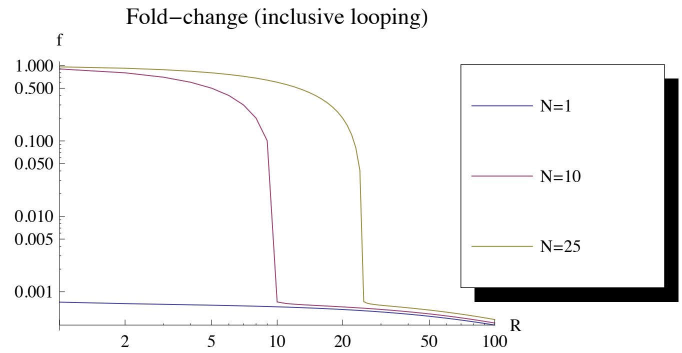
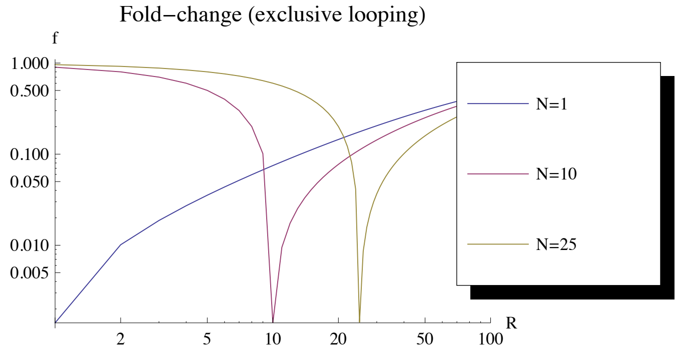
```
Needs["PlotLegends`"]


(* MODEL PARAMETERS *)
(* - - - - - - - - - - *)
Nns = 5.0 * 10^6; (* Number of non-specific binding sites *)
P = 1000;       (* Number of RNAP molecules    *)
Ermd = -17.3;   (* Operator binding energy *)
Epd = -3;        (* RNAP binding energy *)


(* FOLD-CHANGE: SIMPLE REPRESSION *)
(* - - - - - - - - - - - - - - - - - - *)

(* Single promoter partition function *)
Z[0] := 1 + p;
Z[1] := E^(-Ermd);
Z[i_] := 0;

(* Multiple promoter partition function *)
ZtotID[F_, 0] = 1;
ZtotID[F_, n_] := Sum[Multinomial[k1, n - k1]
     F! / (F - k1)! / Nns^k1 Z[0]^(n - k1) Z[1]^k1  , {k1, 0, Min[n, F]}];

(* Fold-change *)
f[F_, n_] :=
  D[Log[ZtotID[F, n]], p] / n / D[Log[ZtotID[0, 1]], p]  /. p → P / Nns * E^(-Epd) ;

(* Plot *)
ListLogLogPlot[{Table[{x, f[x, 1]}, {x, 1, 1000}],
  Table[{x, f[x, 10]}, {x, 1, 1000}], Table[{x, f[x, 100]}, {x, 1, 1000}]},
 Joined → True, PlotRange → {{1, 1000}, {0, 10^-4}},
 PlotLegend → {"N=1", "N=10", "N=100"}, LegendPosition → {0.6, -0.39},
 AxesLabel → {"R", "f"}, PlotLabel → "Fold-change (simple repression)"]
```



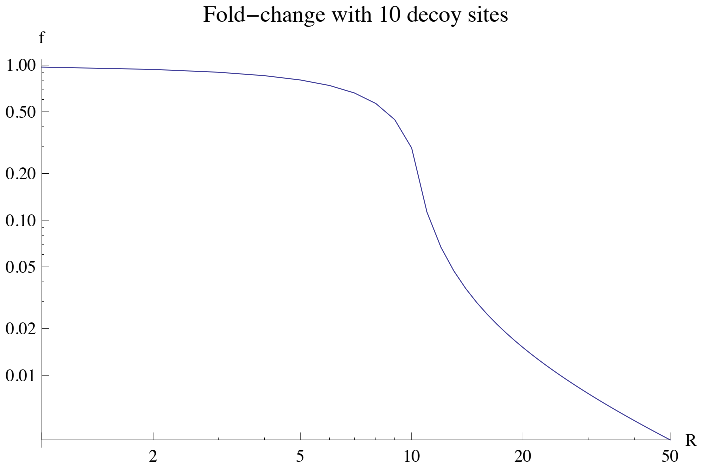
```
(* FOLD-CHANGE: INCLUSIVE LOOPING REPRESSION *)
(* - - - - - - - - - - - - - - - - - - - - - -  *)

Floop = 10;  (* Looping free energy *)
k = 2;       (* k=2 --> both repressor heads bound *)

Z1[0] := 1 + p;
Z1[1]  :=  k Exp[-Ermd] (2 + p) + k Exp[- (2 Ermd + Floop)];
Z1[2]  := k^2 Exp[-2 Ermd];
Z1[n_]  :=  0;
Z[R_, n_] := Sum[Multinomial[k2, k1, n - k1 - k2]
     R! / Nns^(k1 + 2 k2) / (R - k1 - 2 k2) ! Z1[0]^(n - k1 - k2) * Z1[1]^k1 Z1[2]^k2,
    {k2, 0, Min[n, Floor[R / 2]]}, {k1, 0, Min[n - k2, R - 2 k2]}];

f[R_, n_] := D[Log[Z[R, n]], p] / n / D[Log[Z[0, 1]], p]  /. { p → P / Nns * Exp[-Epd]};

ListLogLogPlot[{Table[{x, f[x, 1]}, {x, 1, 100}], Table[{x, f[x, 10]}, {x, 1, 100}],
   Table[{x, f[x, 25]}, {x, 1, 100}]}, Joined → True, PlotRange → {{1, 100}, All},
  PlotLegend → {"N=1", "N=10", "N=25"}, LegendPosition → {0.6, -0.39},
  AxesLabel → {"R", "f"}, PlotLabel → "Fold-change (inclusive looping)"]
```



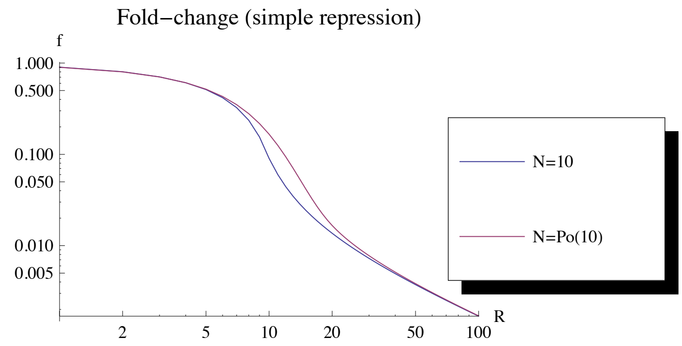
```
(* FOLD-CHANGE: EXCLUSIVE LOOPING REPRESSION *)
(* - - - - - - - - - - - - - - - - - - - - -  *)

k = 2;
Floop = 10;

Z1[0] := 1 + p;
Z1[1] := k Exp[-Ermd] (2 + 2 p) + k Exp[- (2 Ermd + Floop)];
Z1[2] := k^2 Exp[-2 Ermd] (1 + p);
Z1[n_] := 0;
Z[R_, n_] := Sum[Multinomial[k2, k1, n - k1 - k2]
     R! / Nns^(k1 + 2 k2) / (R - k1 - 2 k2)! Z1[0]^(n - k1 - k2) * Z1[1]^k1 Z1[2]^k2,
    {k2, 0, Min[n, Floor[R / 2]]}, {k1, 0, Min[n - k2, R - 2 k2]}];

f[R_, n_] :=
  N[D[Log[Z[R, n]], p] / n / D[Log[Z[0, 1]], p]  /. {p → P / Nns * Exp[-Epd]}];

ListLogLogPlot[{Table[{x, f[x, 1]}, {x, 1, 100}], Table[{x, f[x, 10]}, {x, 1, 100}],
  Table[{x, f[x, 25]}, {x, 1, 100}]}, Joined → True, PlotRange → {{1, 100}, All},
 PlotLegend → {"N=1", "N=10", "N=25"}, LegendPosition → {0.6, -0.39},
 AxesLabel → {"R", "f"}, PlotLabel → "Fold-change (exclusive looping)"]
```



```
(* FOLD-CHANGE: SIMPLE REPRESSION WITH DECOY SITES *)
(* - - - - - - - - - - - - - - - - - - - - - - - -  *)

Epl = -18.5;  (* Binding energy of decoy site *)

Z1[Np_, i_] := Binomial[Np, i] E^(-i Epl);
Z2[0] := 1 + p;
Z2[1] := E^(-Ermd);

Ztot[R_, Np_] = Sum[R! / Nns^(f1 + f2) / (R - f1 - f2) ! Z1[Np, f1] Z2[f2],
   {f1, 0, Min[Np, R]}, {f2, 0, Min[1, R - f1]}];
f2[R_, Np_] := D[Log[Ztot[R, Np]], p] / D[Log[Ztot[0, Np]], p] /.
   p → P / Nns * E^(-Epd) ;

ListLogLogPlot[Table[{i, f2[i, 10]}, {i, 0, 50}],
 Joined → True, PlotRange → {{1, 50}, All}, AxesLabel → {"R", "f"},
 PlotLabel → "Fold-change with 10 decoy sites"]
```



```
(* DISTRIBUTION OF PROMOTER COPY NUMBER: FOLD-CHANGE FOR SIMPLE REPRESSOR *)
(* - - - - - - - - - - - - - - - - - - *)

(* Single promoter partition function *)
Z[0] := 1 + p;
Z[1] := E^(-Ermd);
Z[i_] := 0;

(* Multiple promoter partition function *)
ZtotID[F_, 0] = 1;
ZtotID[F_, n_] := Sum[Multinomial[k1, n - k1]
    F ! / (F - k1) ! / Nns^k1 Z[0]^(n - k1) Z[1]^k1  , {k1, 0, Min[n, F]}];

(* Fold-change *)
f[F_, n_, nmean_] :=
  D[Log[ZtotID[F, n]], p] / nmean / D[Log[ZtotID[0, 1]], p]  /. p → P / Nns * E^(-Epd) ;

(* Note: When considering a distribution of repressor or promoter
  copy numbers one might need to truncate the distribution after some
  number of standard deviations, for computational efficieny. *)

simprepf = Table[{i, f[i, 10, 10]}, {i, 0, 100}]; (* Fold-change, fixed N. *)
simprepfPo10 = Table[
   {i, Sum[PDF[PoissonDistribution[10], j] * f[i, j, 10], {j, 0, 20}]}, {i, 0, 100}];
(* Fold-change, Poisson distribution of promoter copies (mean=10) *)

ListLogLogPlot[{simprepf, simprepfPo10}, Joined → True, PlotRange → {{1, 100}, All},
 AxesLabel → {"R", "f"}, PlotLegend → {"N=10", "N=Po(10)"},
 LegendPosition → {0.6, -0.39}, PlotLabel → "Fold-change (simple repression)"]
```



```
(* TRANSCRIPTIONAL CORRELATION: TWO ACTIVATED GENES *)
(* - - - - - - - - - - - - - - - - - - - - - - - - - - - *)

Eint = -7;  (* Interaction energy RNAP-TF *)
Epd = -5;

Z1[0] := 1 + p1 + p2 + p1 p2;
Z1[1] :=
  Exp[-Ermd] (1 + Exp[-Eint] p1) (1 + p2) + Exp[-Ermd] (1 + p1) (1 + Exp[-Eint] p2);
Z1[2] := Exp[-2 Ermd] (1 + Exp[-Eint] p1) (1 + Exp[-Eint] p2);
Z1[n_] := 0;
Z[R_, n_] := Sum[Multinomial[k2, k1, n - k1 - k2]
     R ! / Nns ^ (k1 + 2 k2) / (R - k1 - 2 k2) ! Z1[0] ^ (n - k1 - k2) * Z1[1] ^k1 Z1[2] ^k2,
    {k2, 0, Min[n, Floor[R / 2]]}, {k1, 0, Min[n - k2, R - 2 k2]}];

(* Correlation coefficient *)
ρ[R_, n_] := p1 p2
     D[Log[Z[R, n]], p1, p2] / (p2 D[Log[Z[R, n]], p2] + p2^2 D[Log[Z[R, n]], p2, p2]) /.
    { p1 → P / Nns * Exp[-Epd], p2 → P / Nns * Exp[-Epd]};

ListPlot[{Table[{R, ρ[R, 5]}, {R, 0, 40}],
  Table[{R, ρ[R, 10]}, {R, 0, 40}], Table[{R, ρ[R, 20]}, {R, 0, 40}]},
 Joined → True, AxesLabel → {"A", "ρ"}, PlotLegend → {"N=5", "N=10", "N=20"},
 PlotRange → All, LegendPosition → {0.6, -0.39} ,
 PlotLabel → "Transcriptional correlation (2 activated genes)"]
```